UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/306,986	05/07/99	TRINH	T 0942.4570001

HM22/0619

STERNE KESSLER GOLDSTEIN & FOX PLLC
ATTORNEYS AT LAW
1100 NEW YORK AVENUE NW SUITE 600
WASHINGTON DC 20005-3934

EXAMINER	
HUTSON,R	
ART UNIT	**PAPER NUMBER**
1652	11

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/306,986	TRINH ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13 and 38-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13 and 38-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Applicants cancellation of claims 1-7 and 14-37 drawn to non-elected inventions, the amendment of claims 8-10 and 12 and the addition of claims 38-55 is acknowledged. Claims 8-13 and 38-55 are at issue and are present for examination.

Applicants' arguments filed on 4/2/2001, paper No. 10, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-13 and 50-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 (9-13 dependent on) is indefinite in that it is unclear and vague in the recitation "a crude preparation containing DNA" because it is unclear what is to be encompassed by "a crude preparation containing DNA". While " preparation containing DNA" appears to be well defined as its literal interpretation, one of skill in the art would not necessarily know how the term "crude" is to be defined and thus this makes a "crude preparation containing DNA" somewhat unclear and therefore the claim is indefinite.

Claim 50 (51-55 dependent on) is indefinite in that it is unclear and confusing in the recitation "wherein said nucleic acid synthesis has not occurred prior to said mixing

(of nucleic acid and DNA polymerase and ribonuclease)". Since the method uses a nucleic acid template, how is it possible that nucleic acid synthesis has not occurred prior to said mixing. Such a limitation precludes the use of a nucleic acid template because this nucleic acid template has to have been the result of "nucleic acid synthesis" and this has to have happened prior to the "mixing".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 38-43, 44-49 and 50-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claim 38 (39-43 dependent from) recites "...wherein the peptide or polypeptide is not Rnase H..." This recitation drawn to a "negative limitation" is not supported by the original specification and therefore is considered new matter.

Newly added claim 44 (45-49 dependent from) recites "... mixing a nucleic acid template which is not cDNA with..." This recitation drawn to a "negative limitation' is not supported by the original specification and therefore is considered new matter.

Newly added claim 50 (51-55 dependent from) recites "... wherein nucleic acid synthesis has not occurred prior to said mixing..." This recitation drawn to a "negative

limitation" is not supported by the original specification and therefore is considered new matter.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 8-12, 38-43 and 50-55 and are rejected under 35 U.S.C. 102(a) as being anticipated by Maudru et al. (Journal of Virological Methods 66: 247-261, July 1997).

The rejection is originally stated as it applies to claims 8-12 in the previous office action.

Applicants traverse this rejection on a number of different basis as it applies to claims 8-12, 38-43 and 50-55.

Applicants traverse this rejection as it applies to claims 8-12 on the basis that claim 8 has been newly amended to require a crude DNA-containing preparation as the starting sample, and applicants point out that Maudru et al. require RNA as the starting material. This argument is not held persuasive because as discussed above it is somewhat unclear what is encompassed by the term "crude DNA-containing preparation and the preparation used by Maudru et al. was a "crude DNA-containing preparation". It is acknowledged that Maudru et al. teach a method that begins with a RNA-containing preparation, but this is converted to a DNA-containing preparation during the reverse transcriptase step. It is at this point where Maudru et al. anticipates the claimed methods in that the starting material is now a DNA containing preparation and in as much as no additional purification steps have been done to this preparation, it

could be considered a "crude DNA-containing preparation". Thus, Maudru et al. continues to anticipate the claimed methods of claims 8-12.

Applicants traverse this rejection as it applies to claims 38-43 on the basis that claim 38 excludes Rnase H as the peptide or polypeptide having ribonuclease activity and applicants assert that the Maudru et al. method relies on the action of Rnase H. This argument is not held persuasive because the Maudru et al. method is not dependent on the action of Rnase H. No where in the reference can it be found that "Rnase H" is mentioned, so it is not understood how the method can be "dependent on the action of Rnase H" . Under the materials and Methods section on page 249, Maudru et al. lists the source of Rnase used as that of Boehringer-Mannheim (Catalog No: 119-915). The Boehringer-Mannheim Catalog lists Catalog No: 119-915, as a "heterogeneous mixture of ribonucleases", not as "Rnase H". Even if this contained Rnase H, which is unclear, their is no indication that the method of Maudru et al. is dependent on Rnase H. Thus , Maudru et al. anticipates the claimed methods of claims 38-43.

Applicants traverse this rejection as it applies to claims 50-55 on the basis that new claims 50-55 require a specific sequence of steps wherein the peptide or polypeptide with ribonuclease activity is added prior to nucleic acid synthesis. and in the Maudru et al. method nucleic acid synthesis begins during the reverse transcriptase step prior to the addition of the Rnase and the DNA polymerase and since therefore nucleic acid synthesis has already occurred, claims 50-55 cannot be anticipated by Maudru et al. This argument is not held persuasive because while Maudru et al. do

teach a method which comprises nucleic acid synthesis prior to the mixing of a nucleic acid template with one or more DNA polymerases and one or more ribonucleases, the taught method of Maudru et al. also comprises a method for synthesizing a nucleic acid molecule, said method comprising mixing a nucleic acid template with one or more DNA polymerases and one or more ribonucleases wherein nucleic acid synthesis occurs after said mixing of the DNA polymerase and ribonuclease. Thus this method within the method taught by Maudru et al. is drawn to a method wherein nucleic acid synthesis has not occurred prior to said mixing. See above 112 2nd paragraph rejection for additional analysis of the claimed method.

7. Claims 8-12 and 50-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Don et al. (Nucleic Acids Research 21(3): page 783, 1993).

The rejection is originally stated as it applies to claims 8-12 in the previous office action.

Applicants traverse this rejection as above, on a number of different basis as it applies to claims 8-12, 38-43 and 50-55.

Applicants traverse this rejection as it applies to claims 8-12 on the basis that claim 8 has been newly amended to require a crude DNA-containing preparation as the starting sample, and applicants point out that Don et al. require purified RNA as the starting material. This argument is not held persuasive because as discussed above it is somewhat unclear what is encompassed by the term "crude DNA-containing preparation and the preparation used by Don et al. was a "crude DNA-containing preparation". It is acknowledged that Don et al. teach a method that begins with a RNA-

containing preparation, but this is converted to a DNA-containing preparation during the reverse transcriptase step. It is at this point where Don et al. anticipates the claimed methods in that the starting material is now a DNA containing preparation and in as much as no additional purification steps have been done to this preparation, it could be considered a "crude DNA-containing preparation". Thus, Don et al. continues to anticipate the claimed methods of claims 8-12. Further to this point, Don et al. actually begin their taught methods with "Cells" which are added to 100 ul of solution D (page 783, column 2, first line of paragraph 2). This surely would be encompassed by a "crude preparation containing".

Applicants traverse this rejection as it applies to claims 50-55 as above, on the basis that new claims 50-55 require a specific sequence of steps wherein the peptide or polypeptide with ribonuclease activity is added prior to nucleic acid synthesis and in the Don et al. method nucleic acid synthesis begins during the reverse transcriptase step prior to the addition of the Rnase and the DNA polymerase and since therefore nucleic acid synthesis has already occurred, claims 50-55 cannot be anticipated by Don et al. This argument is not held persuasive because while Don et al. do teach a method which comprises nucleic acid synthesis prior to the mixing of a nucleic acid template with one or more DNA polymerases and one or more ribonucleases, the taught method of Don et al. also comprises a method for synthesizing a nucleic acid molecule, said method comprising mixing a nucleic acid template with one or more DNA polymerases and one or more ribonucleases wherein nucleic acid synthesis occurs after said mixing of the DNA polymerase and ribonuclease. Thus this method within the method taught by Don

et al. is drawn to a method wherein nucleic acid synthesis has not occurred prior to said mixing. See above 112 2nd paragraph rejection for additional analysis of the claimed method.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 8-13, 38-43, 44-49 and 50-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maudru et al. or Don et al.

As discussed above, Maudru et al. examine the cause and teach a method for the elimination of background signals in a modified polymerase chain reaction-based reverse transcriptase assay and Don et al. teach a "one tube reaction" for synthesis and amplification of total cDNA from a small number of cell.

One of ordinary skill in the art would have been motivated to use both a DNA polymerase and a ribonuclease together for a method of synthesizing a nucleic acid molecule from any nucleic acid template including but not limited to RNA, cDNA or genomic DNA, which encompasses preparations containing either RNA, DNA or both. With respect to Maudru et al. this motivation is suggested in the abstract in which Maudru et al. states that the background signal of the PBRT assay was found to be due to an intrinisic RNA-dependent DNA polymerase activity of the Taq DNA polymerase. Thus their exists motivation for the use of a ribonuclease together with Taq DNA polymerase in any method in which Taq DNA polymerase will be used to synthesize a nucleic acid.

One of ordinary skill in the art would have been motivated to use any of a number of commercially available ribonucleases in the above method, a number of which were available commercially as long as the contaminating RNA was digested. As was discussed above Maudru et al. used a commercially available Rnase that contained a heterogeneous number of RNases.

Further, one of ordinary skill in the art would have been motivated to use the method of claim 10 to synthesize a nucleic acid molecule wherein one or more of said nucleotides are detestably labeled so that the synthesized DNA molecule could be used as a probe to isolate similar DNA molecules from a DNA library, or so that the label could be used as a means of measuring the amount of DNA synthesized. One would have had a reasonable expectation of success based on the knowledge well known in the art of using radioactive nucleotides in DNA synthesis reactions to detestably label the synthesized product.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

ELIZABETH SLOBODYANSKY, PH.D.
PRIMARY EXAMINER

Richard Hutson Ph.D.
June 18, 2001